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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/084,380	02/28/2002	Daniel G. Chain	27580-0003001	3496

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EXAMINER	
EMCH, GREGORY S	

ART UNIT	PAPER NUMBER
1649	

NOTIFICATION DATE	DELIVERY MODE
05/03/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/084,380	CHAIN, DANIEL G.	
	Examiner	Art Unit	
	GREGORY S. EMCH	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 January 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14,19,20,25,55,56,72,75 and 93-116* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14,19,20,25,55,56,72,75 and 93-116* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01/19/2011*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 19 January 2011 has been entered.

Claims 14, 19, 20, 25, 55, 56, 72, 75 and 93-116 are under examination in the instant office action.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 19 January 2011 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 14, 19, 20, 25, 55, 56, 93-98 and 105-108 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Becker et al. (EP 0 613 007, published 31 August 1994; Citation N on PTO-892 dated 27 May 2009) and further in view of Audia et al. (US 5,965,614; issued 12 October 1999; effective priority date of 22 November 1996; Citation A on PTO-892 dated 27 May 2009).

Becker teaches the use of conformationally-specific antibodies and antibody fragments which bind to amyloid β (Aβ) peptides for the treatment of amyloid accumulation diseases, such as Alzheimer's disease. Some of these antibodies bind selectively with those Aβ peptides, which are predominantly in a β-sheet conformation and some of the antibodies bind to Aβ peptides, which have adopted a random coil or α-helix conformation (col.5, lines 42-50; col.7, lines 49-52). Becker teaches that such antibodies would be useful in inhibiting the neurotoxicity associated with the accumulation of oligomeric Aβ in Alzheimer's disease (col.1, lines 1-18; col.5, lines 27-41). Becker teaches antibodies that bind to dissociated (i.e., soluble Aβ, including Aβ 1-40) and those that bind to aggregated Aβ, wherein administration of both types of antibodies is therapeutically effective in treating the neurotoxicity associated with

Alzheimer's disease (col.2, lines 38-50; col.5, lines 42-50; col.7, lines 49-52), as in claims 14 and 20. Becker teaches monoclonal antibodies, humanized antibodies, chimeric antibodies, antibody binding fragments (including Fab, $F(ab')_2$ and Fv fragments) and single-chain antibodies (col.5, line 50 – col.6, line 12), as in claims 19, 25, 55, 56, 93-98 and 105-108. It is noted that the active method steps of independent claims 14, 20 and 105 are essentially the same, i.e. said claims require contacting an Aβ peptide with an exogenous free-end specific antibody in the cerebrospinal fluid (CSF) of an Alzheimer's patient. The contacting steps in these claims are taught by Becker, since Becker teaches administration of the antibodies for therapeutic treatment of Alzheimer's disease patients, which would necessarily reach the cerebrospinal fluid of the patients (see e.g. col.8, lines 16-42). That is, the active step recited in the claims is administering (in general) and does not require administration to the CSF. The claims are construed to encompass any route of administration, and since Becker teaches that the method is sufficient to treat Alzheimer's, the antibodies must reach the CSF. It is noted that the instant specification (see paragraphs [0010], [0043], and [0090]) indicates that the methods can include routes of administration other than directly to the CSF. Since the antibodies would necessarily reach the CSF and bind the Aβ peptide therein, Becker inherently teaches a method of obtaining an amyloid β-peptide-antibody complex which comprises forming a composition consisting essentially of: an Aβ antibody, cerebrospinal fluid and said Aβ peptide, as in claims 93-98. Becker does not explicitly teach contacting *in vivo* soluble Aβ in the cerebrospinal fluid of an Alzheimer's

patient with an exogenous free-end specific antibody which is targeted to a free N-terminus or a free C-terminus of Aβ 1-40.

However, Audia teaches that the Aβ monoclonal antibody 3D6 binds specifically to residues 1-5 of Aβ and that said antibody does not recognize secreted amyloid precursor protein (APP) or full-length APP, but detects Aβ species with an amino terminal aspartic acid, i.e. at position 1 of Aβ peptide (col.49, lines 21-24), as in claims 55, 56, 93-98 and 105-108. Audia's antibody is "free-end specific" as instantly claimed, since it does not bind to APP (see description at e.g. p.8, lines 10-17 of the specification). Audia does not teach administration of the free end specific antibody for inhibiting accumulation and neurotoxicity associated with Alzheimer's disease.

It would have been *prima facie* obvious to the artisan of ordinary skill in the art at the time the invention was made to arrive at the claimed invention by combining the disclosures of Becker and Audia. The artisan would have been motivated to use the 3D6 antibody, i.e. which is a free-end specific antibody directed to the N-terminus of Aβ, in Becker's therapeutic methods because Audia teaches that said antibody is highly specific for Aβ and does not cross react with other closely related molecules, such as APP. That is, since Becker teaches that administration of any Aβ antibody would be useful to treat Alzheimer's disease and Audia teaches that the 3D6 antibody specifically targets the art-recognized peptide involved in the neuropathology of said disease, it would be obvious to use Audia's antibody in Becker's therapeutic methods. Thus, the artisan would have had a reasonable expectation of success that the 3D6 antibody would be successful in treating the neurotoxicity associated with Alzheimer's disease,

since it specifically targets Aβ, which is associated with the neurotoxicity in Alzheimer's disease.

Claims 14, 19, 20, 25, 55, 56, 93-98 and 105-108 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Becker et al. (EP 0 613 007, published 31 August 1994; Citation N on PTO-892 dated 27 May 2009), further in view of Audia et al. (US 5,965,614; issued 12 October 1999; effective priority date of 22 November 1996; Citation A on PTO-892 dated 27 May 2009) and as evidenced by Johnson-Wood et al. (PNAS, Feb. 1997, citation AO on IDS dated 03 June 2002).

It is noted that the instant rejection is virtually identical to the rejection set forth above but with further motivation provided by the prior art reference by Johnson-Wood. Becker et al. teach as set forth above but do not explicitly teach contacting *in vivo* soluble Aβ in the cerebrospinal fluid of an Alzheimer's patient with an exogenous free-end specific antibody which is targeted to a free N-terminus or a free C-terminus of Aβ 1-40.

Audia teaches that the Aβ monoclonal antibody 3D6 binds specifically to residues 1-5 of Aβ and that said antibody does not recognize secreted amyloid precursor protein (APP) or full-length APP, but detects Aβ species with an amino terminal aspartic acid, i.e. at position 1 of Aβ peptide (col.49, lines 21-24), as in claims 55, 56, 93-98 and 105-108. Audia's antibody is "free-end specific" as instantly claimed, since it does not bind to APP (see description at e.g. p.8, lines 10-17 of the specification). Audia does not

teach administration of the free end specific antibody for inhibiting accumulation and neurotoxicity associated with Alzheimer's disease.

It would have been *prima facie* obvious to the artisan of ordinary skill in the art at the time the invention was made to arrive at the claimed invention by combining the disclosures of Becker and Audia. The artisan of ordinary skill would have been motivated to use the 3D6 antibody, i.e. which is a free-end specific antibody directed to the N-terminus of Aβ, in Becker's therapeutic methods because Audia teaches that said antibody is highly specific for Aβ and does not cross react with other closely related molecules, such as APP. That is, since Becker teaches that administration of Aβ antibodies would be useful to treat Alzheimer's disease and Audia teaches that said antibody specifically targets the art-recognized peptide involved in the neuropathology of said disease, it would be obvious to use Audia's antibody in Becker's therapeutic methods. Furthermore, Johnson-Wood teaches that 3D6 is free-end specific (p. 1551, first column, section on Abeta measurement), and that it binds to amyloid plaques very well (see Figure 4 and p. 1553, paragraph spanning the 2 columns). This guides the artisan of ordinary skill to select 3D6 based on its superior ability to bind the plaques known to be associated with Alzheimer's disease. Thus, the artisan of ordinary skill would have had a reasonable expectation of success that the 3D6 antibody would be successful in treating the neurotoxicity associated with Alzheimer's disease, since it specifically targets Aβ and blinds to Aβ plaques, which are associated with the neurotoxicity in Alzheimer's disease.

Claims 14, 19, 20, 25, 72, 75, 99-104 and 109-116 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Becker et al. (EP 0 613 007, published 31 August 1994) and further in view of Mak et al. (Polyclonals to beta-amyloid(1-42) identify most plaque and vascular deposits in Alzheimer cortex, but not striatum. Brain Res. 1994 Dec 19;667(1):138-42; Citation U on PTO-892 dated 27 May 2009).

As set forth above, Becker teaches the use of conformationally-specific antibodies and antibody fragments which bind to Aβ peptides for the treatment of amyloid accumulation diseases, such as Alzheimer's disease. Some of these antibodies bind selectively with those Aβ peptides, which are predominantly in a β-sheet conformation and some of the antibodies bind to Aβ peptides, which have adopted a random coil or α-helix conformation (col.5, lines 42-50; col.7, lines 49-52). Becker teaches that such antibodies would be useful in inhibiting the neurotoxicity associated with the accumulation of oligomeric Aβ in Alzheimer's disease (col.1, lines 1-18; col.5, lines 27-41). Becker teaches antibodies that bind to dissociated, (i.e., soluble Aβ, including Aβ 1-40) and those that bind to aggregated Aβ, wherein administration of both types of antibodies is therapeutically effective in treating the neurotoxicity associated with Alzheimer's disease (col.2, lines 38-50; col.5, lines 42-50; col.7, lines 49-52), as in claims 14 and 20. Becker teaches monoclonal antibodies, humanized antibodies, chimeric antibodies, antibody binding fragments (including Fab, $F(ab')_2$ and Fv fragments) and single-chain antibodies (col.5, line 50 – col.6, line 12), as in claims 19, 25, 99-104 and 109-120. It is noted that the active method steps of independent claims 14, 20, 109, 113 and 117 are essentially the same, i.e. said claims require contacting an

Aβ peptide with an exogenous free-end specific antibody in the cerebrospinal fluid of an Alzheimer's patient. The contacting step in these claims are taught by Becker, since Becker teaches administration of the antibodies for therapeutic treatment of Alzheimer's disease patients, which would necessarily reach the cerebrospinal fluid of the patients (see e.g. col.8, lines 16-42). That is, the active step recited in the claims is administering (in general) and does not require administration to the CSF. The claims are construed to encompass any route of administration, and since Becker teaches that the method is sufficient to treat Alzheimer's, the antibodies must reach the CSF. It is noted that the instant specification (see paragraphs [0010], [0043], and [0090]) indicates that the methods can include routes of administration other than directly to the CSF. Since the antibodies would necessarily reach the CSF and bind the Aβ peptide therein, Becker inherently teaches a method of obtaining an amyloid β-peptide-antibody complex which comprises forming a composition consisting essentially of: an Aβ antibody, cerebrospinal fluid and said Aβ peptide, as in claims 99-104. Becker does not explicitly teach contacting *in vivo* soluble Aβ in the cerebrospinal fluid of an Alzheimer's patient with an exogenous free-end specific antibody which is targeted to a free C-terminus of Aβ 1-40, as in claims 72, 75, 99-104 and 109-120.

Mak teaches that polyclonal antibodies which are raised to Aβ 34-40 are capable of binding to Aβ 1-40, but not to Aβ 1-42 (see p.138, abstract and second paragraph). Since the antibodies do not bind to a longer form of Aβ (Aβ 1-42), the antibodies would not bind to APP either, since APP contains Aβ 1-42. It is noted that Mak teaches that the antibody "was predominantly reactive against β40 and was specific for β40 after

absorption on β42" (p. 138, 2nd paragraph). It would be obvious to the artisan to perform the same method steps for purification of the antibody and use said antibody after it has been purified (as in the cited portion of Mak's disclosure). This would result in an antibody that is more specifically targeted to the Aβ 1-40 peptide, which Mak teaches is involved in disease pathology. Mak does not teach administration of the free end specific antibody for inhibiting accumulation and neurotoxicity associated with Alzheimer's disease.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to arrive at the claimed invention by combining the disclosures of Becker and Mak. The artisan of ordinary skill would have been motivated to use the antibodies to Aβ 34-40, i.e. which is a free end-specific antibody directed to the C-terminus of Aβ 1-40, in Becker's therapeutic methods. This is because Mak teaches that said antibodies are highly specific for Aβ 1-40, that this peptide is involved in the neuropathology of Alzheimer's disease, and that this peptide is the major species present in the CSF (see p.138, first paragraph). Further, Mak suggests that the C-terminus of Aβ may be an important variable in Alzheimer's disease pathology (see p.138, first paragraph). Thus, the artisan would be motivated to use antibodies to Aβ 34-40 to attempt to treat Alzheimer's disease. Moreover, given that Becker teaches monoclonal antibodies and other chimeric antibodies, it would be obvious for the artisan of ordinary skill to generate a monoclonal antibody from Mak's polyclonals. Thus, the artisan would have had a reasonable expectation of success that the antibodies to Aβ

34-40 would be successful in treating the neurotoxicity associated with Alzheimer's disease.

Declaration under 37 CFR 1.132

The declaration under 37 CFR 1.132 filed on 19 January 2011, i.e., the Relkin declaration, is insufficient to overcome the outstanding rejections under 35 U.S.C. 103 (a).

Item (12) of the declaration states that a person of ordinary skill in the art in April 1997 would have recognized that Becker's methods explicitly required the use of antibodies selective for specific amyloid β conformations and that the 3D6 monoclonal antibody and modifications of Mak's anti-serum would not have been recognized in April 1997 to have conformational specificity. The declarant states that in view of Becker's clear teaching of the importance of conformational specificity, a person of ordinary skill in the art in April 1997 would not have used the Audia antibody or a modification of the Mak anti-serum in Becker's methods because they would not have believed there was reasonable likelihood that the combined teachings would be successful in treating Alzheimer's disease. Item (17) of the declaration states that a person of ordinary skill in the art in April 1997 would have understood that when Becker refers to "antibodies of the invention" it refers to conformation specific anti-β amyloid peptide antibodies, to the exclusion of anti-β amyloid peptide antibodies that lack conformation specificity. The declarant states that one of ordinary skill in the art would have understood that Becker's statement, "The antibodies of the present invention are especially preferred in the

diagnosis and/or treatment of Alzheimer's disease," referred in its broadest aspect to conformation-specific anti-β amyloid antibodies, and most preferably to antibodies that are specific for β amyloid peptide in the β-sheet conformation. Item (24) of the declaration states that Becker also makes mention of antibodies that recognize Aβ in the α-helical or random coil conformation. The declarant states that in April 1997, almost all anti-β amyloid antibodies were characterized on the basis of their binding to linear epitopes within the primary sequence of the Aβ molecule, not by recognition of specific higher order conformations and that Becker thus does not teach that "any" Aβ antibody can be used to treat Alzheimer's disease. Item (28) of the declaration states that Johnson-Wood uses the 3D6 antibody to detect β amyloid in fixed thin sections and that the β amyloid in formalin fixed thin sections in Johnson-Wood was chemically modified and would not necessarily have been expected to retain its native conformations. The declarant states that the Examiner asserts that Johnson-Wood demonstrates 3D6 binds to amyloid plaques "very well" or with "superior ability" but that Johnson-Wood did not provide a comparison of plaque binding of 3D6 relative to other anti-β amyloid antibodies available at that time. Item (34) states that one of ordinary skill in the art in April 1997 would have understood that Aβ40 is less likely to be the pathogenic agent of Alzheimer's disease, based on the observations in Mak that Aβ40 is a minor component of plaques, notwithstanding that it is "the major" Aβ species in normal CSF; and, as contrasted by Mak with Aβ42, is more readily cleared; and is less prone to accumulate in cells.

Applicant's arguments have been fully considered and are not found persuasive. Becker teaches treating Alzheimer's disease with multiple types of antibodies (whether they are conformation-specific or not) and the Johnson-Wood reference provides motivation to select 3D6 in that it binds to plaques in tissue. Given that Becker teaches treating Alzheimer's disease with antibodies, given that multiple antibodies are disclosed to work and given that Becker does not provide specific antibodies, one of ordinary skill in the art would look to other references for guidance as to which antibodies to select. Accordingly, Johnson-Wood discloses a desirable antibody because it binds to the pathological form of Aβ within human tissue, i.e. the Aβ in the β-sheet confirmation, which Becker discloses as the most pathological form of Aβ. Moreover, a recent decision by the Board of Patent Appeals and Interferences affirmed the examiner's rejection under 35 U.S.C. 103(a), wherein Becker was the primary reference (as in the instant rejections under 35 U.S.C. 103(a)) and wherein a secondary reference disclosed an antibody raised against a linear epitope (as in the 3D6 antibody). This finding of obviousness thus disclosed an analogous rejection to the instant rejections in that Becker teaches that multiple types of antibodies to Aβ would be effective for treating Alzheimer's disease and that the secondary reference teaches an antibody raised against a linear epitope (see Decision on Appeal dated 22 February 2011 in U.S. application serial no. 10/923,469, especially pp.6-13). Therefore, the instant rejections are also deemed proper for the more general implications disclosed by Becker as set forth above.

Regarding Johnson-Wood, regardless of whether the tissue sections have been subjected to formalin, the 3D6 antibody was still capable of binding to plaques in native tissue. The statement by the examiner that 3D6 binds plaques well is evidenced by Figure 4 and p. 1553, paragraph spanning the 2 columns. Figure 4 shows the progression of staining in PDAPP mice (a transgenic mouse model of Alzheimer's disease) at 4, 8, 10, 12, 16 and 18 months of age. Here, the staining of Aβ plaques consistently increases with age, where at 10 months of age, many large Aβ deposits are found throughout the frontal and cingulate cortex and the molecular layers of the hippocampus. Johnson-Wood teaches, "The outer molecular layer of the dentate gyrus receiving perforant pathway afferents from the entorhinal cortex is clearly heavily delineated by Aβ deposition. This general pattern was more pronounced by heavier Aβ deposition at 1 year of age, and by 18 months of age it involves most of the neocortex. Notably, a striking increase in Aβ plaque burden paralleled the rising Aβ levels" (compare Figs. 2A (ELISA results) and 4). Given that the staining of plaques was so pronounced (especially in older animals), this is interpreted by the examiner as 3D6 binding plaques very well, whether or not 3D6 was compared to any other Aβ antibody.

Regarding Mak, at p.138, first sentence, Mak states, "Deposition of a 28-43 amino acid peptide, β-protein (Aβ) accompanies Alzheimer's disease (AD)." The abstract of Mak also states that a purified antibody to residues 34-40 of Aβ preferentially recognizes Aβ40 and binds to vascular amyloid and a subset of plaques. Therefore, regardless of whether Mak teaches that Aβ42 may be more prevalent in Alzheimer's

plaques, Mak still provides motivation to target Aβ40 since Mak teaches that Aβ40 is involved in Alzheimer's disease pathology.

Response to Arguments

Most of applicant's arguments reiterate the assertions provided in the Relkin declaration and will not be repeated here. Selected statements, which have not been addressed above will be addressed herein. In the reply filed on 19 January 2011, applicant asserts that with respect to a finite number of identified predictable solutions that leads to anticipated success, the Relkin declaration reports that many anti-Aβ antibodies had been developed by the time of filing. Applicant asserts that the only rationale provided by the examiner as to why it would have been obvious to use a free end-specific antibody is that such an antibody would recognize Aβ but not other closely related molecules such as APP. Applicant asserts that as pointed out by Dr. Relkin, the prior art fails to support provide any advantage of this property in a therapeutic antibody. Applicant asserts that the Examiner has therefore failed to provide a legitimate rationale for choosing a free end-specific antibody from among all Aβ antibodies that were known and that an obvious to try rationale thus fails because the 3D6 antibody and the anti-40 antibody were not chosen from a finite number of possibilities.

Applicants' arguments have been fully considered and are not found persuasive. Choosing an antibody that binds to a 38-43 amino acid residue protein from a number of antibodies disclosed in the prior art is considered choosing from a finite number of identified predictable solutions. The number of antibodies disclosed in the prior art at

the time of filing is indeed finite, even if there was a number of antibodies disclosed. The prior art supports the predictability that antibodies to Aβ would be useful in treating Alzheimer's disease, contrary to applicant's assertion. Just because there are multiple therapeutic possibilities for treatment (multiple antibodies) does not negate any one of these possibilities (a particular antibody). Further, in response to applicant's argument that there is no teaching, suggestion, or motivation to combine the references, the examiner recognizes that obviousness may be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988), *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992), and *KSR International Co. v. Teleflex, Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007). In this case, it would have been common sense for one of ordinary skill in the art to recognize that an antibody that binds to the pathogenic component of a disease, i.e. to the protein that is implicated in the disease (in this case Aβ), but that does not bind to other closely related proteins (in this case APP) would be highly preferred for treatment of the particular disease. Antibody specificity is highly important for treatment and this is indeed in the knowledge generally available to one of ordinary skill in the art.

Conclusion

No claims are allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached 9:00 am - 5:30 pm EST (M-F).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ali Salimi, can be reached at (571) 272-0909. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.
/G.E./

Gregory S. Emch
Patent Examiner
Art Unit 1649
27 April 2011

/DANIEL E. KOLKER/
Primary Examiner, Art Unit 1649
April 28, 2011